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(71) Applicant *(for all designated States except US)*: MINNESOTA MINING AND MANUFACTURING COMPANY [US/US]; 3M Center, P.O. Box 33427, Saint Paul, MN 55133-3427 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: KUESTER, Wilhelm [DE/DE]; Girmes-Kreuz-Strasse 68, D-41564 Kaarst (DE). D'HAESE, François, C. [BE/BE]; Brabantdam 130, B-Gent (BE). KANTNER, Steven, S. [US/US]; 1203 Laurel Avenue, St. Paul, MN 55104 (US).

(74) Agents: HORNICKEL, John, H. et al.; Minnesota Mining and Manufacturing Company, Office of Intellectual Property Counsel, P.O. Box 33427, Saint Paul, MN 55133-3427 (US).

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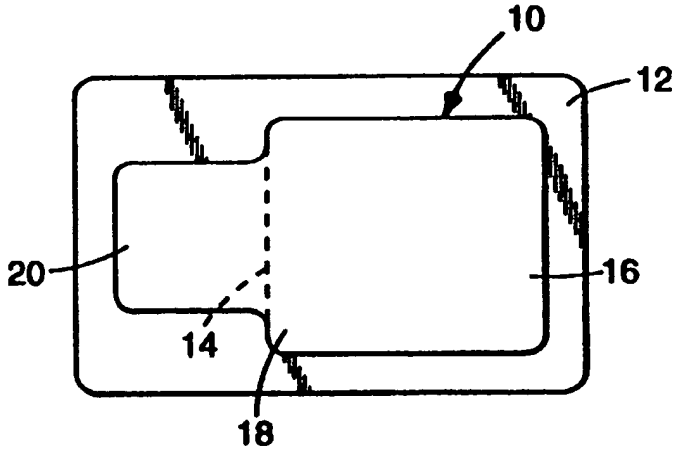
(54) Title: USE OF PENDANT PHOTOREACTIVE MOIETIES ON POLYMER PRECURSORS TO PREPARE HYDROPHILIC PRESSURE SENSITIVE ADHESIVES

(57) Abstract

Crosslinked, hydrophilic pressure sensitive adhesives prepared from precursors and medical products using such adhesives are disclosed. The crosslinked polymer is prepared by free-radically photocrosslinking reactive polymers that are functionalized with pendant photoreactive moieties. Medical products that include such compositions are biomedical electrodes, pharmaceutical delivery devices, and medical skin coverings such as wound dressings.



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USE OF PENDANT PHOTOREACTIVE MOIETIES ON POLYMER PRECURSORS TO PREPARE HYDROPHILIC PRESSURE SENSITIVE ADHESIVES

Field of the Invention

This invention relates to hydrophilic pressure sensitive adhesives, polymer precursors to them that have pendant photoreactive moieties, and medical products using such adhesives.

Background of the Invention

Hydrophilic pressure sensitive adhesives are used in the medical field for a variety of skin-contacting applications as detailed in "An Overview of Skin Contact Applications for Pressure-sensitive Adhesives", D.G. Pierson, Tappi Journal, 73 (6), 101-107 (June, 1990). These applications include use as adhesives which absorb exudate from wounds, as ionically conductive adhesives in biomedical electrodes, and in iontophoretic (electrically enhanced) transdermal delivery of polar drugs.

Hydrophilic pressure sensitive adhesives are networks of a polar polymer, generally crosslinked and plasticized with a compatible humectant material such as glycerin or poly(ethylene glycol). Water, a salt, or a drug may also be included depending on the application. A relatively thick layer of adhesive is typically used (0.25 to 2.5 mm (10 to 100 mil) or greater).

Several approaches have been developed to prepare these hydrophilic pressure sensitive adhesives. They can be generated by delivering a moderate viscosity solution from solvent or water and drying (exemplified by US 5,276,079); by extrusion coating a high viscosity precursor (exemplified by US 4,674,512 and US 4,593,053); by polymerization on-web of a low viscosity mixture of monomer, crosslinker, and humectant (exemplified by US 4,524,087; US

4,539,996; US 4,554,924; and US 4,848,353); and by crosslinking on-web a moderate viscosity precursor of polymer and humectant. For this final approach the crosslinking can be brought about by exposure of a non-functional polymer to high energy irradiation (exemplified by US 4,699,146; US 4,750,482; and WO 93/10163), by mixing in a reactive crosslinking agent during the coating process (exemplified by US 4,515,162; US 5,160,328; and WO 93/22380), or by exposure of a vinyl functional polymer to a free radical source. Such vinyl functional polymers can be prepared by reaction of amine terminated poly(ethylene oxide) with, for example, vinyl dimethyl azlactone (WO 94/12585), reaction of isocyanate functional polyoxyalkylene oligomer with hydroxyethyl methacrylate (EP 271,292), and reaction of poly(vinyl ether/maleic anhydride) with allyl amine or allyl alcohol (GB 2,268,495). These approaches are applicable to a relatively narrow range of polar polymers and may require the use of an aprotic solvent during synthesis which must be removed.

Summary of the Invention

A need exists for a method of photoactivated crosslinking of polar polymers which can be applied to a wider range of materials and that does not require specialized equipment or the use of aprotic solvent, yielding materials that can be rapidly and reliably crosslinked without generating concerns about potentially toxic or irritating unreacted low molecular weight monomers.

A need also exists for materials which allow for efficient manufacture of medical articles and devices in an integrated fashion, reducing the number of steps required and hence reducing waste and expense.

This invention concerns polar polymers which are prepared via thermal polymerization with copolymerizable pendant photoreactive moieties that undergo activation to provide crosslinked hydrophilic pressure sensitive adhesives when plasticized with humectants. When this pendant photoactive moiety is obtained from a "system soluble", (meth)acrylated photoinitiator , very rapid, reproducible, and complete crosslinking can be obtained with high intensity UV

lights allowing for efficient manufacture of adhesive coated articles and tapes, especially when thick coatings of adhesive are desired. These materials are particularly suited for use as skin contacting pressure sensitive adhesives for medical use where high moisture vapor transmission rates or ionic conductivity may be important.

"System soluble" means that the photoinitiator is soluble in a mixture of water, plasticizer, and monomer at a temperature used in copolymerization. .

Thus, this invention provides a family of hydrophilic pressure sensitive adhesives based on plasticized polar networks. These networks are prepared by free-radically photocrosslinking reactive polymers which are functionalized with pendant photoinitiators.

This invention has several advantages. The precursor is low viscosity, readily processable and coatable, and solventless. No additional mixing or compounding of the precursor is required. The crosslink density is predetermined. The adhesives can rapidly and reliably be prepared without requiring specialized equipment and without generating concerns about potentially toxic or irritating unreacted low molecular weight monomers.

In one aspect of the invention, the method of functionalization involves reaction of a system soluble acrylated photoinitiator with monomer(s) to give photoreactive pendant moieties from the polymer backbone.

In another aspect of the invention, novel pressure sensitive adhesives are obtained by exposing a mixture of a polar polymer functionalized with pendant photoreactive moieties and a plasticizer compatible with this polymer to ultraviolet light energy. In order for the resulting swollen network to possess a degree of pressure sensitive tack, the functionalized polar polymer should be present in an amount of about 10 to 40 weight percent with plasticizer being present in amount of about 90 to 60 weight percent.

If too little functionalized polar polymer is present, difficulty could be encountered in crosslinking the composition to obtain adequate cohesive

strength. If too much functionalized polar polymer is present, the resulting network could have too high a modulus to possess adhesive properties.

Similarly, the degree of functionalization of the polar polymer can impact adhesive properties since it determines the crosslink density of the resulting network. If there are too many pendant photoreactive moieties, a brittle, tack free elastomer could result. If there are too few pendant photoreactive moieties, cohesive strength could be compromised.

The polar polymer can contain from about 95 weight percent to 99.5 weight percent, preferably 97 weight percent to 99 weight percent, hydrophilic monomer and from 0.5 weight percent to 5 weight percent, preferably 1 to 3 weight percent, of system soluble (meth)acrylated photoinitiator.

In another aspect of the present invention, the pressure sensitive adhesive composition can be used in a medical device requiring pressure sensitive adhesiveness to mammalian skin. Often, additional ingredients are included, and the pressure sensitive adhesive must be compatible with them.

For example, pressure sensitive adhesives used in transdermal drug delivery devices may also serve as a reservoir for the drug. Pressure sensitive adhesives used in wound dressings may require high moisture vapor transmission rates to prevent skin maceration and aid healing. Pressure sensitive adhesives used in biomedical electrodes may need to be ionically-conductive.

Another advantage of the pressure sensitive adhesive compositions of the present invention is their ability to be used in biomedical electrodes, wound dressings, and transdermal drug delivery devices.

For a greater appreciation of the invention, embodiments of the invention are described with reference to the following drawings.

Brief Description of the Drawings

Fig. 1 is a top plan view of a biomedical electrode containing an adhesive composition of the present invention, used for diagnosis or monitoring of heart conditions of a mammalian patient.

Fig. 2 is a cross-sectional view of the biomedical electrode of Fig. 1.

Fig. 3 is a top plan view of a monitoring biomedical electrode containing an adhesive composition of the present invention, used for longer term diagnosis or monitoring of heart conditions.

Fig 4 is a cross-sectional view of the monitoring biomedical electrode of Fig. 3.

Fig. 5 is a cross-sectional view of another monitoring biomedical electrode containing an adhesive compositon of the present invention and a stud connector.

Fig. 6 is a sectional view of a medical mammalian skin covering containing adhesive composition of the present invention.

Fig. 7 is a sectional view of a pharmaceutical delivery device containing an adhesive composition of the present invention.

Embodiments of the Present Invention

Polar Polymer

The polar polymer forms the backbone of the polymeric matrix of the pressure sensitive adhesive composition. The polymer can be formed by copolymerizing the (meth)acrylated photoinitiator with free-radically copolymerizable monomers. .

Nonlimiting examples of useful polar monomers used to form such polymers include:

carboxylic acids, (e.g., acrylic acid, carboxyethyl acrylate, itaconic acid, fumaric acid, maleic acid, or methacrylic acid (and their ammonium, lithium, potassium, or sodium salts)); ammonium or metal salts of sulfonic or phosphonic acids (e.g., 2-sulfoethyl methacrylate, 3-sulfopropyl acrylate, 2-acrylamido-2-methylpropane sulfonic acid, styrene sulfonic acid, vinyl benzyl phosphonic acid); amides (e.g., acrylamide, methacrylamide, N,N-dimethyl acrylamide, and N-vinyl pyrrolidone); ethers (e.g., 2-ethoxyethyl acrylate and 2-methoxyethyl methacrylate); monomers having hydroxyl functi nality (e.g., 2-hydroxyethyl acrylate, 2-

hydroxyethyl methacrylate, and dihydroxy propylacrylate); or ammonium functionality derived from reaction of amine containing monomers (e.g., N,N-dimethyl aminoethyl methacrylate and vinyl pyridine) with alkylating agents.

One skilled in the art will recognize that moderate levels of non-polar monomers, such as alkyl acrylates and methacrylates of from 4 to 16 carbon atoms or vinyl and isopropenyl carboxylates, can be useful in these copolymers to impart cohesive strength and limit moisture sensitivity without having a detrimental effect on the compatibility of the copolymer with polar plasticizer.

These polymers can be synthesized by standard free-radical solution polymerization methods as outlined in Sorenson and Campbell, Preparative Methods of Polymer Chemistry, Second Edition, John Wiley & Sons, 1968.

Homopolymers of acrylic acid and methacrylic acid and their alkali metal salts and copolymers of acrylic acid and its alkali salts with acrylamide or N-vinyl pyrrolidone are currently preferred because they give acceptable performance.

Photoreactive Moieties

The polar polymers described above are functionalized with photoreactive moieties by copolymerization of a system soluble, copolymerizable photoinitiator during polymerization of the polymer.

A specific acrylated derivative of benzophenone, namely: p-acryloyloxybenzophenone disclosed in European Patent Publication 0 246 848 or U.S. Pat. Nos. 4,737,559 or 4,847,137 is not a system soluble copolymerizable photoinitiator according to the definition of "system soluble".

Nonlimiting examples of such photoinitiators include water soluble derivatives of photoactive benzophenones, acetophenones, or photoinitiable (meth)acrylates. Of these photoinitiators, quarternized ammonium photoactive benzophenones are especially preferred because of their excellent water solubility to aid processing. In the event the polar polymer is based on (meth)acrylic acid or its derivatives, a water soluble acrylated photoactive benzophenone is especially preferred. Ketones described in U.S. Pat. No. 4,948,819 are useful to be derivatized to provide water solubility for use as photoinitiators in the present

invention. Particularly preferred photoinitiators are (2-acryloyloxy)(4-benzoylbenzyl) dimethylammonium bromide commercially available as "Quantacure ABQ" from Octel Chemicals of London, U.K.; 4-(2-acryloyloxyethoxy)-phenyl(2-hydroxy-2-propyl)-ketone commercially available as "ZLI 3331" from Ciba-Geigy of Basel, Switzerland; and 2-acryloyloxyethoxyethoxy-4-chloro-2'-carboxybenzophenone commercially available as "Uvecryl P36" from Radcure of Drogenbos, Belgium.

Generally the polar monomer is present in large molar excess, ensuring that all the copolymerizable photoinitiator is reacted to form pendant moieties on the backbone of the polar polymer. Desirably, the molar ratio of polymer to copolymerizable photoinitiator ranges from about to 1000:1 to about 50:1. . Preferably, the molar ratio of polymer to polymerizble photoinitiator ranges from about 500:1 to about 100:1.

Thermal polymerization initiator can be used to aid in the polymerization of monomers to form the polymer having pendant photoreactive moieties for ultraviolet energized crosslinking. Suitable thermal initiators can be selected from the group of inorganic peroxides such as hydrogen peroxide and alkali metal peroxide disulfates. Further, azo compounds and acyl peroxides are useful. It is obvious to those skilled in the art to select a suitable polymerization initiator from those being commercially available and to use them in an amount providing a prepolymer having a desired molecular weight. Preferably, the thermal polymerization initiator is present in an amount from about 0.01 to about 0.05 weight percent.

Plasticizer

The plasticizer serves to increase the compliance of the crosslinked polymer composition to provide adhesive properties and conformability. The plasticizer also serves to modify the tack or thumb appeal of the crosslinked polymer composition. The plasticizer can also also serve as a solvent to dissolve other additives including electrolytes, and pharmacologically active components.

The plasticizer can also serve as a means to drop the glass transition temperature and therefore enable the polar polymer to become a pressure sensitive adhesive.

Using water alone as the plasticizer could yield compositions with poor to moderate tack which are prone to rapid loss of moisture and a concomitant change into a leathery or glassy material when exposed to ambient conditions.

Hence useful plasticizers are those selected from the group consisting of alcohols, mixtures of alcohols, and mixtures of water and alcohols such that the mixture of plasticizer and carboxy-functional polymer is liquid in the uncrosslinked state and displays pressure sensitive tack in the crosslinked state.

The plasticizer can comprise from about 10 weight percent to 100 weight percent water and from 0 weight percent to about 90 weight percent alcohol.

Nonlimiting alcohols for the polar polymers described above include glycerin, propylene glycol, dipropylene glycol, sorbitol, 1,3-butanediol, 1,4-butanediol, trimethylol propane, and ethylene glycol and derivatives given by:

$$MO(CH_2CH_2O)_mH$$

wherein

M is selected from the group consisting of hydrogen and C_1 through C_6 alkyl,

and m is an integer of about 1 to about 25. Of these possible plasticizers, trimethylolpropane is preferred because it minimizes hydrogen abstraction and results in the least number of side reactions during crosslinking.

Optional Surfactants

Anionic, cationic, nonionic or amphoteric surfactants can optionally be used in amounts ranging from about 10 weight percent to about 40 weight percent of the crosslinked composition and preferably from about 15 weight percent to about 35 weight percent of the crosslinked composition.

The use of such surfactants improves the adhesion of the pressure sensitive adhesive electrodes to oily mammalian skin by giving the adhesive lipophilic properties. By incorporating the surfactants into the adhesive

composition, the compatibility between the adhesive and the oily mammalian skin is improved. For example, copending, coassigned United States Patent Application Serial N . _____ (Attorney's Docket 48381____A) incorporated by reference herein, discloses the advantages of using surfactants in pressure sensitive adhesives.

Suitable anionic compatible surfactants include alkyl benzene sulfonates, alkyl sulfonates, olefin sulfonates, alkyl ethersulfonates, glycerol ethersulfonates, α-methyl estersulfonates, sulfonic fatty acids, alkyl sulfates, fatty alcohol ethersulfates, glycerol ethersulfates, mixed hydroxy ethersulfates, monoglyceride (ether)sulfates, fatty acid amide (ether)sulfates, sulfosuccinates, sulfosuccinamates, sulfotriglycerides, amide soaps, ether carboxylic acids, isethionates, sarcosinates, taurides, alkyl oligoglycoside sulfates and alkyl (ether)phosphates.

Suitable nonionic compatible surfactants include fatty alcohol polyglycolethers, alkyl phenylpolyglycolethers, fatty acid polyglycolesters, fatty acid amide polyglycolethers, fatty amine polyglycolethers, alkoxylated triglycerides, alk(en)yl oligoglycosides, fatty acid glucamides, polyol fatty acid esters, sugar esters, sorbitol esters and sorbitol ester ethoxylates and polysorbates.

Suitable cationic compatible surfactants include quaternary ammonium compounds and quaternized difatty acid trialkanol amine esters.

Preferred compatible surfactants may be selected from nonionic surfactants having an HLB-value of 10 to 17. Fatty alcohol polyglycolethers, sorbitol fatty acid esters, and sorbitol fatty ester ethoxylates in this HLB range are particularly preferred. As is known to those skilled in the art, the HLB-value is an acronym for the hydrophilic-lipophilic balance and indicates the extent to which a given surfactant will behave as an oil-soluble vs. a water-soluble type of emulsifier as described in Chapter 20 of Surface Active Agents and Detergents, Volume II, Anthony M. Schwartz, James W. Perry, and Julian Berch, Robert E. Krieger Publishing Co., Huntington, New York, 1977. HLB-values in this range help assure that the surfactant is soluble in the adhesive formulation and also have high enough hydrocarbon content to impart desired oil absorbancy at lower usage.

Optional Processing Additives

Additives can also be incorporated into the composition including low levels of copolymerizable vinyl monomers, crosslinkers, and non-functionalized compatible polymers.

Low levels of copolymerizable vinyl monomers, particularly those miscible in the reactive polymer/plasticizer mixture, can serve to accelerate the rate of crosslinking. Preferred copolymerizable monomers include acrylic acid and methacrylic acid and their ammonium and alkali metal salts, N-vinyl pyrrolidone, acrylamide, 2-acrylamido-2-methyl propane sulfonic acid and its ammonium and alkali metal salts, hydroxyethyl acrylate, hydroxyethyl methacrylate, 2-ethoxyethyl acrylate, 2-ethoxyethyl methacrylate, and 2-(2-ethoxyethoxy)ethyl acrylate. When utilized, the amount of copolymerizable vinyl monomer preferably comprises from about 2 to about 15 weight percent of the total adhesive composition.

Addition of non-functionalized compatible polymers is contemplated as a means of enhancing the viscosity of the precursor prior to cure to impart better coatability for, for example, pattern coating of the adhesive. Suitable polymers include those that are hydrophilic and compatible in the reactive polymer/plasticizer mixture including moderate and high molecular weight poly(ethylene oxide), poly(acrylic acid), poly(N-vinyl pyrrolidone), poly(vinyl alcohol), and poly(acrylamide).

Additional crosslinkers can be desired for use in the present invention. Suitable crosslinkers include triethylene-glycol-bismethacrylate (TEGBM), ethylene-glycol-bismethacrylate, methylene bisacrylamde, tetraethylene-glycol-bismethacrylate, methylene bisacrylamide, tetraethylene-glycol-diacrylate (TEGDA), and 3,3'-ethylidene-bis (N-vinyl-2-pyrrolidone). The amount of the crosslinker can be varied. Preferred crosslinker levels range from about 0.2 weight percent to about 0.9 weight percent of the total adhesive composition.

Optional Water Absorbing Compounds

Pressure sensitive adhesive compositi ns of the present invention can also contain water absorbing compounds that have the ability to absorb body fluids such as perspiration and exudate from mammalian skin to decrease the loss of adhesion of the composition in the presence of wet mammalian skin.

Nonlimiting examples of water absorbing compounds useful for the present invention include natural polysaccharides (e.g., karaya gum and agar-agar); crosslinked dextran; cellulose and modified cellulose polymers; starch and synthetically modified starch polymers; guar gum; pectin; gelatin; carrageenan; and crosslinked poly (vinyl lactams) prepared according to U.S. Pat. No. 5,362,420 (Itoh et al.), the disclosure of which is incorporated herein.

Additives for Biocompatible and/or Therapeutic and/or Ionically-Conductive Uses

Depending upon the use of the hydrophilic, pressure sensitive adhesive of the present invention, various biocompatible and/or therapeutic and/or materials that provide ionic conductivity can be included in the adhesive.

For example, adhesives of the present invention can be used as conductive adhesive in a biomedical electrode with the addition of an ionically-conductive electrolyte to the adhesive. Nonlimiting examples of electrolyte include ionic salts dissolved in the adhesive to provide ionic conductivity and can include magnesium acetate, magnesium sulfate, sodium acetate, sodium chloride, lithium chloride, lithium perchlorate, sodium citrate, and preferably potassium chloride to enhance ionic conductivity of the hydrophilic pressure sensitive adhesive.

Alternatively, a redox couple such as a mixture of ferric and ferrous salts such as sulfates and gluconates can be added.

The amounts of these ionic salts present in adhesives of the present invention are relatively small, from about 0.5 to 7 percent by weight of the adhesive, and preferably about 2 to 5 weight percent. When a redox couple is used, the biomedical electrode can recover from an overload potential. U.S. Pat. No.

4,846,185 (Carim) discloses a redox couple totalling not more than about 20 percent by weight of the adhesive.

Hydr philic, pressure sensitive adhesives of the present invention can also be used in the delivery of pharmaceuticals to or through mammalian skin, such as topical or transdermal drug delivery systems. The pharmaceutical or other active ingredient can be compounded with the adhesive after polymerization, minimizing any possible deleterious interaction of the pharmaceutical or active ingredient with the polymerizing process.

A type of therapeutic procedure both involving application of electrical current to skin of a patient and a pharmaceutical is iontophoresis, which delivers an iontophoretically active pharmaceutical to or through mammalian skin with aid of an electrical current.

The hydrophilic, pressure sensitive adhesive can also be used in therapeutic mammalian skin coverings, such as dressings, wound closure materials, tapes, and the like. Preferably, for mammalian skin covering uses, other biologically active materials can be added to the adhesive of the present invention after polymerization without deleteriously affecting the biologically active material. Nonlimiting examples of such other biologically active materials include broad spectrum antimicrobial agents where it is desired to reduce bacteria levels to minimize infection risk or treat the effects of infections at the skin or skin openings of a mammalian patient. Broad spectrum antimicrobial agents are disclosed in U.S. Pat. No. 4,310,509, which disclosure is incorporated by reference. Nonlimiting examples of other antimicrobial agents include parachlorometaxylenol; triclosan; chlorhexidine and its salts such as chlorhexidine acetate and chlorhexidine gluconate; iodine; iodophors; poly-N-vinyl pyrrolidone-iodophors; silver oxide, silver and its salts, antibiotics (e.g., neomycin, bacitracin, and polymyxin B). Antimicrobial agents can be included in the adhesive after polymerization in a weight from about 0.01 percent to about 10 percent by weight of the total adhesive.

Other biocompatible and/or therapeutic materials can be added to the adhesive such as compounds to buffer the pH of the adhesive to provide a non-irritating pH for use with sensitive mammalian skin tissue or to otherwise maximize

antimicrobial activity. Also, penetration enhancing agents or excipients can be added to the adhesive when the pharmaceutical or other active agent for topical or transdermal delivery so requires.

Method of Preparation

The formation of the polymer with the pendant photoreactive moieties can be conducted in the presence of some or all of the plasticizer. As detailed in the Examples below, a typical preparation involves the polymerization of monomers used to form a polar polymer in the presence of the copolymerizable photoinitiator and thermal initiator and optional surfactant, additives, water absorbing compounds etc.

The reaction is substantially complete within one hour at 70°C and the resulting solution can be diluted further with plasticizer as required.

Crosslinking of the reactive polymer/plasticizer precursor mixture is accomplished by exposing it to photoactivation conditions to permit the photoreactive pendant moieties to generate free radicals for crosslinking between adjoining polymers.

Suitable light sources to effect this crosslinking include medium pressure mercury lamps emitting light at a wavelength of about 253 nm. Light energy reaching the uncrosslinked composition should range from about 100 mJ/cm^2 to about 1500 mJ/cm^2 and preferably from about 250 mJ/cm^2 to about 1000 mJ/cm^2 UV energy.

The reactive polymer/plasticizer mixture can be coated via any of a variety of conventional coating methods, such as roll coating, knife coating, or curtain coating, or can be extruded. The low viscosity allows for injection into cavities of, for example, a monitoring ECG electrode, or pattern coating of the adhesive precursor is possible, particularly with viscosity enhancement.

The polymer/plasticizer precursor can be coated directly on to the flexible substrate of choice including metal foils and metallized polymeric films for conductive adhesives, or can be coated and crosslinked on a release liner to yield a transfer adhesive. In this latter application it can be desirable to embed a tissue

paper or non-woven fabric scrim, such as a 0.1 mm Cerex™ material from Monsanto Chemical Company in the precursor to allow for ease of handling.

Crosslinking is preferably accomplished with the exclusion f oxygen, either in an inert atmosphere such as nitrogen or argon, or by covering the precursor with a non-oxygen permeable film. This film cover should be substantially transparent to the wavelengthsused for photocrosslinking.

Usefulness of the Invention

Adhesive compositions of the present invention can be used in a variety of applications where pressure sensitive adhesives are industrially or commercially applied in the manufacture of tapes, adhesive substrates, and the like. Preferably, adhesive compositions of the present invention can be used in the field of health care where adhesive requirements are particularly stringent and difficult and efficient manufacturing is desired.

Because mammalian skin is a particularly difficult surface to identify and control acceptable adhesive properties, the adhesive composition of the present invention is particularly suitable for use in mammalian skin covering applications such as biocompatible medical adhesives such as for receipt or delivery of electrical signals at or through mammalian skin, delivery of pharmaceuticals or active agents to or through mammalian skin, or treatment of mammalian skin or mammalian skin openings against the possibilities of infection.

Biomedical Electrodes

Biomedical electrodes employing adhesive compositions of the present invention having electrolyte contained therein are useful for diagnostic (including monitoring) and therapeutic purposes. In its most basic form, a biomedical electrode comprises a conductive medium contacting mammalian skin and a means for electrical communication interacting between the conductive medium and electrical diagnostic, therapeutic, or electrosurgical equipment.

FIGS. 1 and 2 show either a disposable diagnostic electrocardiogram (ECG or EKG) or a transcutaneous electrical nerve stimulation (TENS) electrode 10 on a release liner 12. Electrode 10 includes a field 14 of a biocompatible and adhesive conductive medium for contacting mammalian skin of a patient upon removal of protective release liner 12. Electrode 10 includes means for electrical communication 16 comprising a conductor member having a conductive interface portion 18 contacting field 14 of conductive medium and a tab portion 20 extending beyond field 14 of conductive medium for mechanical and electrical contact with electrical instrumentation (not shown). Means 16 for electrical communication includes a conductive layer 26 coated on at least the side 22 contacting field 14 of conductive medium.

It is foreseen that a typical conductor member 16 will comprise a strip of material having a thickness of about 0.05-0.2 millimeters, such as polyester film and have a coating 26 on side 22 of silver/silver chloride of about 2.5-12 micrometers, and preferably about 5 micrometers thick thereon. Presently preferred for conductor member 16 are polyester films commercially available as Scotchpak™ brand film from Minnesota Mining and Manufacturing Company of St. Paul, MN or "Melinex" 505-300, 329, or 339 brand film from ICI Americas of Hopewell, VA. coated with a silver/silver chloride ink commercially available as "R-300" ink from Ercon, Inc. of Waltham, MA. A TENS conductor member 16 can be made of a nonwoven web, such as a web of polyester/cellulose fibers commercially available as "Manniweb" material from Lydall, Inc. of Troy, NY and have a carbon ink layer 26 commercially available as "SS24363" ink from Acheson Colloids Company of Port Huron, MI on side 22 thereof. To enhance mechanical contact between an electrode clip (not shown) and conductor member 16, an adhesively-backed polyethylene tape can be applied to tab portion 20 on the side opposite side 22 having the conductive coating 26. A surgical tape commercially available from 3M Company as "Blenderm" tape can be employed for this purpose.

Alternatively, conductor member can be a multi-layered construction of a nonconductive, flexible polymeric film having a sulfur-reactive surface, a metallic layer deposited on and interacting with the surface and an optional metallic

halide layer, according to the disclosure of PCT Publication WO 94/026950, the disclosure of which is incorporated by reference herein. The conductive interface portion 18 of member 16 comprises a metallic layer deposited on a sulfur-reactive surface on at least the side of polymeric film substrate facing field 14 of the conductive medium and the optional metallic halide layer coated on the metallic layer and contacting field 14. Because depolarizing is not needed for the mechanical and electrical contact with electrical equipment, the optional metallic halide layer does not need to extend to tab portion 20.

Alternatively, conductor member 16 can be a multi-layered construction of a nonconductive, flexible polymeric film, an electrically conductive layer, and a thin, conformable depolarizing layer of inorganic oxide, preferably manganese dioxide. Alternatively, conductor member 16 is a multi-layered construction of film with electrically conductive and depolarizing layers blended together. Both of these alternative embodiments can be constructed according to the disclosure of PCT International Patent Publication WO 95/20350, the disclosure of which is incorporated by reference herein. The conductive interface portion of member comprises an electrically conductive layer coated on at least the side of polymeric film facing field 14 of conductive medium and the thin, depolarizing layer coated on the electrically conductive layer and contacting field 14. Because depolarizing is not needed for the mechanical and electrical contact with electrical equipment, the depolarizing layer does not need to extend to tab portion 20.

Non-limiting examples of biomedical electrodes which can use adhesive compositions of the present invention, either as conductive or non-conductive adhesive fields include electrodes disclosed in U.S. Pat. Nos. 4,524,087; 4,539,996; 4,554,924; 4,848,353 (all Engel); 4,846,185 (Carim); 4,771,783 (Roberts); 4,715,382 (Strand); 5,012,810 (Strand et al.); and 5,133,356 (Bryan et al.), the disclosures of which are incorporated by reference herein.

In some instances, the means for electrical communication can be an electrically conductive tab extending from the periphery of the biomedical electrodes such as that seen in U.S. Pat. No. 4,848,353 or can be a conductor member extending through a slit or seam in an insulating backing member, such as

that seen in U.S. Pat. No. 5,012,810. Otherwise, the means for electrical communication can be an eyelet or other snap-type connector such as that disclosed in U.S. Pat. No. 4,846,185. Further, the means for electrical communication can be a lead wire such as that seen in U.S. Pat. No. 4,771,783. Regardless of the type of means for electrical communication employed, an adhesive composition of the present invention, containing an electrolyte, can reside as a field of conductive adhesive on a biomedical electrode for diagnostic (including monitoring), therapeutic, or electrosurgical purposes.

Another type of diagnostic procedure which can employ a biomedical electrode of the present invention is the longer term monitoring of electrical wave patterns of the heart of a patient to detect patterns of abnormality. A preferred biomedical electrode structure is disclosed in U.S. Pat. No. 5,012,810 (Strand et al.) which is incorporated by reference. The adhesive of the present invention can be used as the ionically conductive medium in any of the embodiments shown therein. Preferably, the adhesive of the present invention is used as the field of conductive adhesive in the biomedical electrode of the embodiment shown in Figs. 2, 3, and 4 of U.S. Pat. No. 5,012,810.

Figs. 3 and 4 substantially correspond to Figs. 2 and 3, respectively, of U.S. Pat. No. 5,012,810. Electrode 40 includes an insulator construction 41, and a conductor member 42.

The insulator construction 41 includes first and second sections 44 and 45 which, together, define opposite sides 46 and 47 of the insulator construction 41. As seen in Fig. 3, each section 44 and 45 includes an elongate edge portion 50 and 51, respectively. The edge portions 50 and 51 each include a border portion 52 and 53, respectively, which comprise a peripheral portion of each section 44 and 45, respectively, and extending along edges 50 and 51, respectively. In that manner, sections 44 and 45 are oriented to extend substantially parallel to one another, with edge portions 50 and 51 overlapping one another such that border portions 52 and 53 overlap. A seam 60 is created between edge portions 50 and 51. "Substantially parallel" does not mean that the sections 44 and 45 are

necessarily precisely parallel. They may be out of precise coplanar alignment due, for example, to the thickness of the conductor member 42.

Conductor member 42 is substantially similar to biomedical electrical conductor 16 described above, having a tab portion 61 corresponding to tab portion 20 described above and a pad portion 62 corresponding to conductive interface portion 18 described above. Like biomedical electrical conductor member 16, conductor member 42 can be any of the embodiments disclosed above. In this embodiment, conductor member 42 is a multi-layered construction of a nonconductive, flexible organic polymer substrate 63 having an organosulfur surface 64, a metallic layer 65 adhered thereto, and, optionally, a metallic halide layer 66, produced according to the disclosure of PCT Patent Publication WO 94/-26950.

The pad portion 62 of member 42 comprises the portion of the metallic film facing field 70 of conductive adhesive, optionally with metallic halide layer 66 contacting field 70. Because depolarizing is not needed for the mechanical and electrical contact with electrical equipment, metallic halide layer 66 need not extend to tab portion 61. Optionally, an adhesively-backed polyethylene tape can be applied to tab portion 61 in the same manner as that for the embodiment of Figs. 1 and 2 in order to enhance mechanical contact.

In general, electrode 40 is constructed such that tab portion 61 of conductor member 42 projects through seam 60 and over a portion of surface or side 46. As a result, as seen in Figs. 3 and 4 pad portion 62 of conductor member 42 is positioned on one side 46 of insulator construction 41, and the tab portion 61 of conductor member 42 is positioned on an opposite side 46 of insulator construction 41. It will be understood that except where tab portion 61 extends through seam 60, the seam may be sealed by means of an adhesive or the like.

As seen in Fig. 4, lower surface 68 of tab portion 61 is shown adhered in position to section 45, by means of double-stick tape strip 69. That is, adhesion in Fig. 4 between the tab portion 61 and section 45 is by means of adhesive 69 underneath tab portion 61.

In Fig. 4, a field 70 of conductive adhesive of the present invention is shown positioned generally underneath conductive member 42. Optionally, field 70 of conductive adhesive will be surrounded by a field 71 of biocompatible skin adhesive also applied to insulator construction 41 the side thereof having pad portion 62 thereon.

In Fig. 4, a layer of release liner 75 is shown positioned against that side of electrode 40 which has optional skin adhesive 71, conductive adhesive 70 and pad portion 62 thereon. Optionally as shown in Fig. 4, a spacer 76 or tab 76 can be positioned between release liner 75 and a portion of insulator construction 41, to facilitate the separation.

A variety of release liners 75 may be utilized; for example, a liner comprising a polymer such as a polyester or polypropylene material, coated with a silicone release type coating which is readily separable from the skin adhesive and conductive adhesive.

A variety of materials may be utilized to form the sections 44 and 45 of the insulator construction 41. In general, a flexible material is preferred which will be comfortable to the user, and is relatively strong and thin. Preferred materials are polymer foams, especially polyethylene foams, non-woven pads, especially polyester non-wovens, various types of paper, and transparent films. Nonlimiting examples of transparent films include polyester film such as a "Melinex" polyester film commercially available from ICI Americas, Hopewell, VA having a thickness of 0.05 mm and a surgical tape commercially available from 3M Company as "Transpore" unembossed tape.

The most preferred materials are non-woven pads made from melt blown polyurethane fiber, which exhibit exceptional flexibility, stretch recovery and breathability. Melt blown polyurethane materials usable in insulator construction 41 in electrodes according to the present invention are generally described in European Patent Publication 0 341 875 (Meyer) and corresponding U.S. Pat. No 5,230,701 (Meyer et al.), incorporated herein by reference.

Optionally the insulator construction has a skin adhesive on its surface contactin~ the remainder of the electrode 40.

Preferred web materials (melt blown polyurethanes) for use in insulator construction 41 have a web basis weight of about 60-140 g/m^2 (preferably about 120 g/m^2). Such materials have an appropriate tensile strength and moisture vapor transmission rate. A preferred moisture vapor transmission rate is about 500-3000 grams water/m^2/24 hours (preferably 500-1500 grams water/m^2/24 hours) when tested according to ASTM E96-80 at 21°C and 50% relative humidity. An advantage to such materials is that webs formed from them can be made which exhibit good elasticity and stretch recovery. This means that the electrode can stretch well, in all directions, with movement of the subject, without loss of electrode integrity and/or failure of the seal provided by the skin adhesive. Material with a stretch recovery of at least about 85%, in all directions, after stretch of 50% is preferred.

It will be understood that a variety of dimensions may be utilized for the biomedical electrode disclosed herein. Generally an insulator construction of about 3.5-4.5 cm by 5.5-10 cm will be quite suitable for typical foreseen applications.

It will also be understood that a variety of materials may be utilized as the skin adhesive. Typically, acrylate ester adhesives will be preferred. Acrylate ester copolymer adhesives are particularly preferred. Such material are generally described in U.S. Pat. Nos. 2,973,826; Re 24,906; Re 33,353; 3,389,827; 4,112,213; 4,310,509; 4,323,557; 4,732,808; 4,917,928; 4,917,929; and European Patent Publication 0 051 935, all incorporated herein by reference.

In particular, an adhesive copolymer having from about 95 to about 97 weight percent isooctyl acrylate and from about 5 to about 3 percent acrylamide and having an inherent viscosity of 1.1-1.25 dl/g is presently preferred.

Adhesive useful for adhesive 69 can be any of the acrylate ester adhesives described above in double stick tape form. A presently preferred adhesive is the same adhesive as presently preferred for the skin adhesive except having an inherent viscosity of about 1.3-1.45 dl/g.

It will be understood that the dimensions of the various layers, and their conformation during association, are shown somewhat exaggerated in Fig. 4,

to facilitate an understanding of the construction. In general, an overall substantially flat appearance with only a very minor "s" type bend in the conductive member 42 is accommodated by the arrangement, despite the multi-layered construction of member 42.

Another biomedical electrode construction is shown in Fig. 5 in cross-section. Electrode 80 has a nonconductive backing 82 having an opening 83 covered by snap 84 though which stud or eyelet 85 protrudes. The snap 84 is secured to eyelet 85 to provide a point of electrical connection to electrical instrumentation. Covering eyelet 84 and backing 82 is a field 86 of the adhesive of the present invention. A release liner 88 protects the PSA field 86 prior to use. Backing 82 can be made of the same or similar materials as insulator construction 41. Eyelet 85 can be a plastic, metallic plated eyelet (such as an ABS plastic eyelet silver-plated and chlorided and commercially available from Micron Products of Fitchburg, MA). Snap 84 can be a metallic snap (such as stainless steel eyelet No. 304 commercially available from Eyelets for Industry of Thomason, CN).

Other examples of biomedical electrodes which can use the present invention as a conductive adhesive include electrodes disclosed in U.S. Pat. No. 4,527,087; 4,539,996; 4,554,924; 4,848,353 (all Engel); 4,846,185 (Carim); 4,771,783 (Roberts); 4,715,382 (Strand); 5,133,356 (Bryan et al.), the disclosures of which are incorporated by reference herein. Methods of making such electrodes are disclosed in such patents, except that adhesive of the present invention can be substituted for the field of conductive adhesive. Among these various electrode constructions is an electrode construction particularly preferred as that shown in FIGS. 4 and 5 of U.S. Pat. No. 4,848,353 (Engel) in which the electrically conductive adhesive 36 is replaced by the adhesive of the present invention.

When used for diagnostic EKG procedures, electrodes shown in Figs. 1 and 2 or those electrodes shown in U.S. Pat. No. 4,539,996 are preferred. When used for monitoring electrocardiogram (ECG) procedures, electrodes shown in Figs. 3 and 4 and those disclosed in U.S. Patent Nos. 4,539,996, 4,848,353, 5,012,810 and 5,133,356 are preferred.

In some instances, the biomedical electrical conductor can be an electrically conductive tab extending fr m the periphery of the biomedical electrodes such as that seen in U.S. Pat. No. 4,848,353 r can be a conductor member extending through a slit or seam in a insulating backing member, such as that seen in U.S. Patent No. 5,012,810. Otherwise, the means for electrical communication can be an eyelet or other snap-type connector such as that disclosed in U.S. Pat. No. 4,846,185. Alternatively, an electrically conductive tab such as that seen in U.S. Pat. No. 5,012,810 can have an eyelet or other snap-type connector secured thereto.

Medical Skin Coverings

Medical skin coverings employing adhesive compositions of the present invention, optionally having antimicrobial and other biologically active agents contained therein, are useful for treatment of mammalian skin or mammalian skin openings, preferably against the possibility of infection and also for the transmission of moisture vapor and exudate from skin.

FIG. 6 shows a sectional view of a medical skin covering 90 having a backing material 92, a layer 94 of adhesive of the present invention coated on backing material 92, and protected until use by a release liner 96. Preferably, antimicrobial 98 is contained in layer 94 by adding agent 98 prior to coating on backing material 92. Alternatively, layer 94 can be used as a caulkable sealant according to U.S. Pat. No. 4,931,282 (Asmus et al.), the disclosure of which is incorporated by reference herein.

For use, the release liner 96 is removed and the layer 94 of adhesive of the present invention can be applied to the skin of the patient as a part of a medical tape, a wound dressing, a bandage of general medicinal utility, or other medical device having water absorbing properties.

The adhesive layer 94 may be coated on a layer of backing material 92 selected from any of several backing materials having a high moisture vapor transmission rate for use as medical tapes, dressings, bandages, and the like. Suitable backing materials include those disclosed in U.S. Patents 3,645,835 and

4,595,001, th disclosures of which are incorporated by reference. Other examples of a variety of films commercially available as extrudable polymers include "Hytrel^{R} 4056" and "Hytrel^{R} 3548" branded polyester elastomers available from E.I. DuPont de Nemours and C mpany of Wilmington, Delaware, "Estane" branded polyurethanes available from B.F. Goodrich of Cleveland, Ohio or "Q-thane" branded polyurethanes available from K.J. Quinn & Co. of Malden, Massachusetts.

The layer 94 of adhesive of the invention combined with a layer 92 of suitable backing material can be used as a dressing.

Adhesive compositions of the present invention can be used as discrete gel particles dispersed in a continuous pressure-sensitive adhesive matrix to form a two phase composite useful in medical applications, as described in U.S. Pat. No. 5,270,358, the disclosure of which is incorporated by reference herein.

The adhesive layer 94 can be coated on the backing layer 92 by a variety of processes, including, direct coating, lamination, and hot lamination. The release liner 96 can thereafter be applied using direct coating, lamination, and hot lamination.

The methods of lamination and hot lamination involve the application of pressure, or heat and pressure, respectively, on the layer of adhesive layer 94 to the backing material layer 92. The temperature for hot lamination ranges from about 50°C to about 250°C, and the pressures applied to both lamination and hot lamination range from 0.1 Kg/cm^2 to about 50 Kg/cm^2.

Pharmaceutical Delivery Devices

Pharmaceutical delivery devices employing hydrophilic, pressure-sensitive adhesive compositions of the present invention, optionally having a topical, transdermal, or iontophoretic therapeutic agent and excipients, solvents, or penetration enhancing agents contained therein, are useful for delivery of pharmaceuticals or other active agents to or through mammalian skin.

FIG. 7 shows a sectional view of a transdermal or topical drug delivery device 100 having a backing layer 102, a layer 104 containing adhesive of the present invention coated thereon and protected by a release liner 106. Other

layers can be present between layer 102 and layer 104 to house pharmaceuticals or other therapeutic agents. Otherwise, as shown in FIG. 7, pharmaceutical and other agents 108 are dispersed in adhesive layer 104.

The backing layer 102 can be any backing material known to those skilled in the art and useful for drug delivery devices. Non-limiting examples of such backing materials are polyethylene, ethylene-vinyl acetate copolymer, polyethylene-aluminum-polyethylene composites, and ScotchPak™ brand backings commercially available from Minnesota Mining and Manufacturing Company of St. Paul, Minnesota.

The release liner 106 can be any release liner material known to those skilled in the art. Non-limiting examples of such release liners commercially available include siliconized polyethylene terephthalate films commercially available from H.P. Smith Co. and fluoropolymer coated polyester films commercially available from 3M under the brand ScotchPak™ release liners.

The therapeutic agent 108 can be any therapeutically active material known to those skilled in the art and approved for delivery topically to or transdermally or iontophoretically through the skin of a patient. Non-limiting examples of therapeutic agents useful in transdermal delivery devices are any active drug or salts of those drugs, used in topical or transdermal applications, or growth factors for use in enhancing wound healing. Other therapeutic agents identified as drugs or pharmacologically active agents are disclosed in U.S. Patent Nos. 4,849,224 and 4,855,294, and PCT Patent Publication WO 89/07951.

Excipients or penetration enhancing agents are also known to those skilled in the art. Non-limiting examples of penetration enhancing agents include ethanol, methyl laurate, oleic acid, isopropyl myristate, and glycerol monolaurate. Other penetration enhancing agents known to those skilled in the art are disclosed in U.S. Patent Nos. 4,849,224; and 4,855,294 and PCT Patent Publication WO 89/07951.

The method of manufacturing a transdermal delivery device depends on its construction.

The drug delivery device 100 shown in FIG. 7 can be prepared using the following general method. A solution is prepared by dissolving the therapeutic agent 108 and such ptional excipients as are desired in a suitable solvent and mixed into the precursor prior to forming the composition, during the formation of the composition, or directly into the already formed composition. The resulting loaded adhesive composition is coated on the backing layer 102. A release liner 106 is applied to cover loaded adhesive layer 104.

Other aspects of the present invention are identified in the following examples.

Examples

Preparation Example

After establishing a desired formulation, the water soluble salt and the system soluble copolymerizable photoinitiator are dissolved in 95 % of the final amount of water. A solution of the hydrophilic polymerizable monomer(s) in the polar organic compound/plasticizer is added and the resulting mixture is stirred until it is homogenous. Optionally a surfactant and/or a water absorbing component are then added and the whole mixture is stirred again. The solution is then transferred to a flask with a reflux-condenser and stirrer and flushed with nitrogen. Afterwards, the thermal initiator dissolved in the remaining 5% of water is mixed in.

The prepolymerization reaction is then started by heating the mixture to 60°C. After 3 hours, reaction is complete and the polymer/plasticizer precursor mixture is then coated at a caliper of 0.5 mm to a 75 μm polyester film and covered with a siliconized 75 μm polyester film. This construction is then irradiated 5-20 seconds with a UV lamp (wavelength 450 nm, intensity 1 mW/cm^2, dose 360 mJ/cm^2).

The siliconized polyester film is removed and the adhesive with the remaining polyester film is used to determine its properties.

The following adhesion tests were carried out:

1. Adhesion

a) A 2.5 cm wide strip of adhesive on polyester film was laid with its adhesive side onto a 100 μm coextruded polyethylene film and overrolled twice with a 2 kg roller. The surface consists of high density polyethylene (HDPE).

The strip was peeled from the surface with a speed of 300 mm/min. with an angle of 180° and adhesion was measured with a tensile tester (in N/dm).

Tests were carried out after 1 min and 24 hours storage (dwell time) at room temperature. In some examples the adhesion after 24 hours at 98 % relative humidity was measured.

b) The same tests were carried out with the same polyethylene film that was contaminated with a 5 % solution of olive oil/oleic acid/linoleic acid/squalene (70/15/10/5) in isopropanol by soaking a tissue into the solution and wiping over the HDPE surface. The test strip was applied after the isopropanol had evaporated and the surface was wiped once more with a clean tissue. The amount of contaminant was determined to be 0.03 mg/cm^2. Olive oil is a triglyceride made up of fatty acids including linear saturated C16 (palmitic acid, 14%), mono-unsaturated C18 (oleic acid, 71%), and di-unsaturated C18 (linoleic acid, 10%) as described in The Encyclopedia of Chemical Technology, Fourth Edition, Volume 10, p. 267, John Wiley and Sons, New York, 1993. Thus this mixture of 70% triglyceride, 25% free fatty acid, and 5% squalene approximates both chemically and in concentration skin surface lipids.

c) When quantitative adhesion tests were not performed, qualitative adhesion tests were conducted by those skilled in the art of pressure sensitive adhesive formulation, processing, and usage.

The compositions and peel adhesion for each of the examples are shown in the Tables 1-3. Table 1 shows the performance of system soluble

copolymerizable photoinitiators useful in the present invention compared with water insoluble polymerizable photoinitiators. Table 2 shows the variation in usage of one water soluble copolymerizable photoinitiator, Quantacure ABQ. Table 3 shows the variation possible for this invention with different plasticizers, comonomers, surfactants, crosslinkers, and additional polar polymers.

Table 1 -Examples with Different Photoinitiators

Composition in Weight %	Example 1	2	3	4	5	C1	C2	C3
AA	19.7	19.7	19.7	19.7	19.7	19.7	19.7	19.7
Quantacure ABQ	0.6			0.6				
ZLI 3331		0.6			0.6			
Uvecryl P36			0.6					
ABP						0.6		
Quantacure BTC							0.6	
ACS								0.6
H_2O	39.5	39.5	39.5	39.5	39.5	39.5	39.5	39.5
KCl	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Trimethylolpropane				39.5	39.5			
PEG 300	39.5	39.5	39.5			39.5	39.5	39.5
$K_2S_2O_8$	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Adhesion	good	good	too soft	good	too soft	no	no	no
Solubility of photoinitiator	complete	complete	partly	complete	partly	no	complete	complete
Curing	good	good	fair	very good	fair	no	no	no

AA		Acrylic Acid
PEG 300		Polyethyleneglycol (MW 300)
Quantacure ABQ	available from Octel Chemicals	(2 acryloxy)(4-benzoylbenzyl) dimethylammonium bromide
ZLI 3331	available from Ciba Geigy	4-(2-Acryloxyethoxy)-phenyl(2-hydroxy-2-propyl)-keton
Uvecryl P36	available from Radcure	2-acryloxyethoxyethoxy-4-chloro 2'carboxybenzophenone
ABP		p-acryloxybenzophenone (prepared according to EP 0 246 848)
Quantacure BTC	available from Octel Chemicals	4-Benzoylbenzyltrimethylammoniumchloride
ACS	available from Fluka	Anthraquinone-2-sulfonic acid, sodium salt monohydric

Table 2 - Variation of Amount of Quantacure ABQ

Composition in Weight %	C1	1	2	3	4	5	6	7	C2
AA	19.9	19.8	19.8	19.8	19.8	19.7	19.6	19.5	19.7
Quantacure ABQ	0	0.2	0.3	0.4	0.5	0.6	0.8	1.2	0.6
H_2O	39.7	39.6	39.6	39.6	39.5	39.5	39.2	39.0	39.5
KCl	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Trimethylolpropane	39.7	39.6	39.6	39.6	39.5	39.5	39.2	39.0	39.5
$K_2S_2O_8$	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Irradiation Time (s)	20	15	10	10	5	5	5	5	1
Dose (mJ/cm^2)	1850	1350	900	900	450	450	450	450	90
Peel (N/dm)	no adh.	4.21	4.37	5.06	6.43	5.40	4.36	5.76	no adh.
Internal Strength	visc. sol.	very soft	too soft	too soft	good	very good	good	too hard	visc. sol.

Table 3 - Different Humectants, Comonomers, Surfactants and Additional Polar Polymers or difunctional acrylate (crosslinker)

Composition in Weight %	1	2	3	4	5	6	7	8	9	10	11	12
AA	19.7	19.7	19.7	9.9	17.8	9.9	18.8	19.7	19.7	19.7	15.8	15.8
Acrylamide				9.9								
NVP					2.0	9.9						
IOA							1.0					
Quantacure ABQ	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.3	0.5	0.6	0.6	0.6
H_2O	39.5	39.5	39.5	39.5	39.5	39.5	39.5	39.5	39.5	39.5	39.5	39.5
KCl	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Glycerol			39.5									
PEG 300		39.5						39.5	39.5			
Trimethylolpropane	39.5			39.5	39.5	39.5	39.5			19.7	39.5	39.5
TEGDM								0.02	0.02			
Lamesorb SMS 20										19.7		

Composition in Weight %	1	2	3	4	5	6	7	8	9	10	11	12
Guar Gum											4.0	
Technocel 30/2												4.0
$K_2S_2O_8$	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05

Irradiation Time (s)	5	15	20	5	5	10	5	10	10	10	10	5
Dose (mJ/cm^2)	450	1350	1850	450	450	900	450	900	900	900	900	450
Peel (N/dm)	3.1	3.2	3.9	2.9	5.6	1.9	n. meas.	7.48	4.72	2.5	1.1	3.0
Peel (oil) (N/dm)	<0.2	<0.2	<0.2	<0.2	<0.2	<0.2	<0.2	<0.2	<0.2	0.7	<0.2	<0.2

Lamesorb SMS 20	available from Chemische Fabrik Grunau, Illertissen, Germany	ethoxylated sorbitol fatty acid estar
TEGDM		Triethyleneglycoldimethacrylate
Technocel 30/2	available from CFF (Cellulose Füllstoff Fabrik) Mönchengladbach, Germany	Cellulose Powder

For an appreciation of the scope of the present invention, the claims follow.

What is claimed is:

1. A precursor for a hydrophilic pressure sensitive adhesive comprising: a copolymer of at least one polar, hydrophilic monomer and a system soluble copolymerizable photoinitiator.

2. The precursor of Claim 1, wherein the precursor has pendant photoreactive moieties that can be free-radically photocrosslinked in the presence of a sufficient amount of plasticizer to impart a degree of pressure sensitive tack to form a hydrophilic pressure sensitive adhesive.

3. The precursor of Claim 1, wherein the system soluble copolymerizable photoinitiators comprise (2-acryloyloxy)(4-benzoylbenzyl) dimethylammonium bromide; 4-(2-acryloyloxyethoxy)-phenyl(2-hydroxy-2-propyl)-ketone; and 2-acryloyloxyethoxyethoxy-4-chloro-2'-carboxybenzophenone.

4. The precursor of Claim 1, further comprising sufficient amount of plasticizer to form the hydrophilic pressure sensitive adhesive.

5. The precursor of Claim 1, wherein the monomer is a carboxylic acid selected from the group consisting of acrylic acid, carboxyethyl acrylate, methacrylic acid,and their salts.

6. The precursor of Claim 1, wherein the polar monomer is selected from the group consisting of carboxylic acids and their ammonium or metal salts; ammonium or metal salts of sulfonic or phosphonic acids; amides; ethers; monomers having hydroxyl functionality; and ammonium functionality derived from reaction of amine containing monomers with alkylating agents

7. The precursor of Claim 4, wherein the plasticizer comprises polyhydric alcohols, mixtures of alcohols, or mixtures of water and alcohols.

8. The precursor of Claim 1, wherein the precursor further comprises surfactants, copolymerizable vinyl monomers, non-functionalized compatible polymers, electrolytes, or combinations thereof.

9. The precursor of Claim 1, wherein the precursor further comprises ionic salts, pharmaceuticals, antimicrobial agents, or combinations thereof.

10. The precursor of Claim 4, wherein the monomer comprises acrylic acid; wherein the system soluble copolymerizable photoinitiator comprises (2-acryloyloxy)(4-benzoylbenzyl) dimethylammonium bromide; and wherein the plasticizer comprises trimethylolpropane.

11. A hydrophilic pressure sensitive adhesive formed from the precursor of Claim 10.

12. A method of preparing a crosslinked hydrophilic pressure sensitive adhesive composition, comprising the steps of:

(a) reacting a polar monomer(s) with a system soluble copolymerizable photoinitiator to generate a polymer precursor having pendant photoreactive moieties;

(b) free radically photocrosslinking the polymer precursor in the presence of plasticizer to generate the crosslinked composition.

13. The process according to Claim 12, wherein the free radical photocrosslinking is carried out in the presence of ultraviolet light.

14. The process according to Claim 12, wherein the monomer comprises acrylic acid; wherein the system soluble copolymerizable photoinitiator

comprises (2-acryloyloxy)(4-benzoylbenzyl) dimethylammonium bromide; and wherein the plasticizer comprises trimethylolpropane.

15. A biomedical electrode, comprising:

a field of adhesive conductive medium for contacting mammalian skin and a means for electrical communication for interfacing with the adhesive conductive medium and electrical diagnostic, therapeutic, or electrosurgical instrumentation, the adhesive conductive medium adhered to the means for electrical communication and comprising an adhesive prepared from the precursor identified in Claim 1.

16. The biomedical electrode according to Claim 15, wherein the adhesive conductive medium further comprises an ionic salt electrolyte present in an amount from about 0.5 to about 5 weight percent of the adhesive conductive medium.

17. The biomedical electrode according to Claim 15, wherein the means for electrical communication comprises a conductor member having an interface portion contacting the adhesive conductive medium and a tab portion available for mechanical and electrical contact with the electrical diagnostic, therapeutic, or electrosurgical instrumentation.

18. The biomedical electrode according to Claim 15, wherein the means for electrical communication comprises a conductor member having an eyelet or snap connector contacting the adhesive conductive medium.

19. A mammalian skin covering comprising: an adhesive layer for contacting mammalian skin and backing layer, the adhesive layer adhered to the backing layer and comprising a pressure sensitive adhesive prepared from the precursor identified in Claim 1.

20. The mammalian skin covering according to Claim 19, wherein the adhesive layer further comprises an antimicrobial agent.

21. The mammalian skin covering according to Claim 19, wherein the backing layer comprises a film, substrate, or elastic, porous or breathable woven or nonwoven material.

22. The mammalian skin covering according to Claim 21, wherein the covering comprises a medical tape, a wound dressing, a bandage of general medicinal utility, or a medical device contacting mammalian skin.

23. A pharmaceutical delivery device comprising: an adhesive layer for contacting mammalian skin and a backing layer, the adhesive layer adhered to the backing layer and comprising a pressure sensitive adhesive prepared from a precursor identified in Claim 1.

24. The pharmaceutical delivery device according to Claim 23, wherein the adhesive layer further comprises a topical, transdermal, or iontophoretic therapeutic agent or pharmaceutical.

25. The pharmaceutical delivery device according to Claim 23, wherein the adhesive layer further comprises an excipient, a solvent, or a penetration enhancing agent.

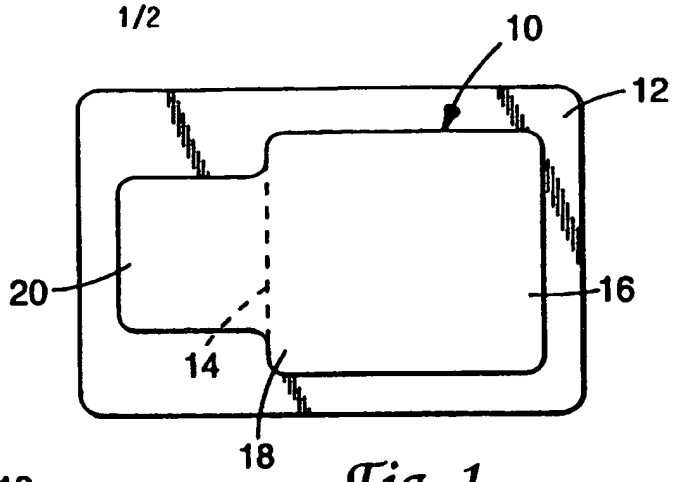

Fig. 1

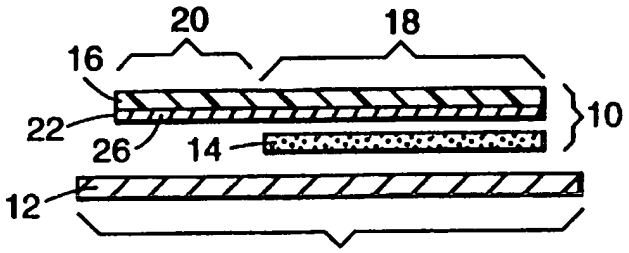

Fig. 2

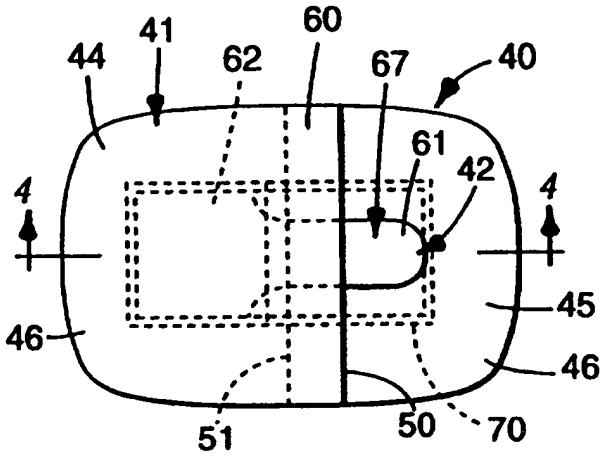

Fig. 3

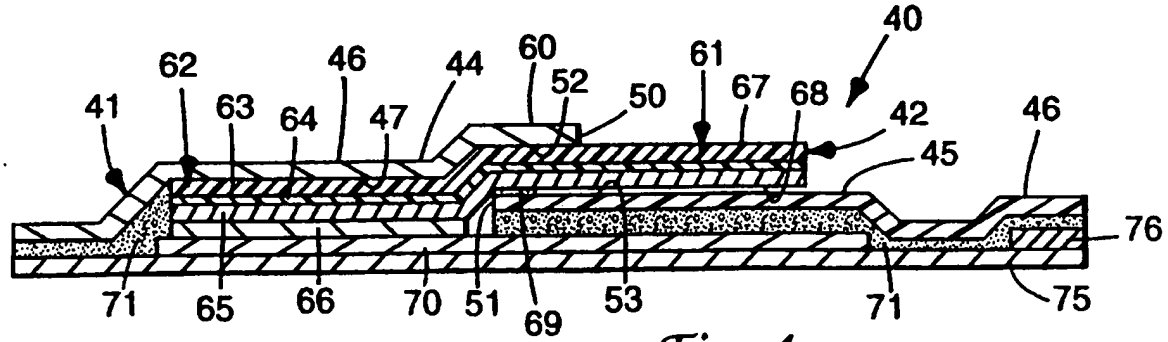

Fig. 4

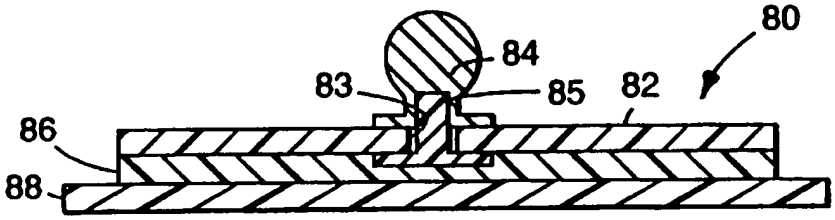

Fig. 5

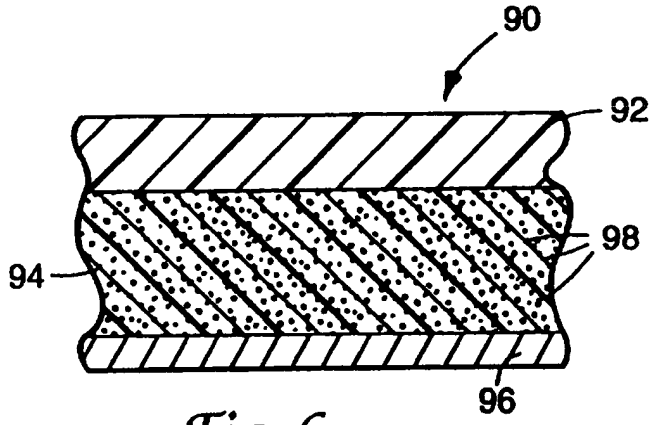

Fig. 6

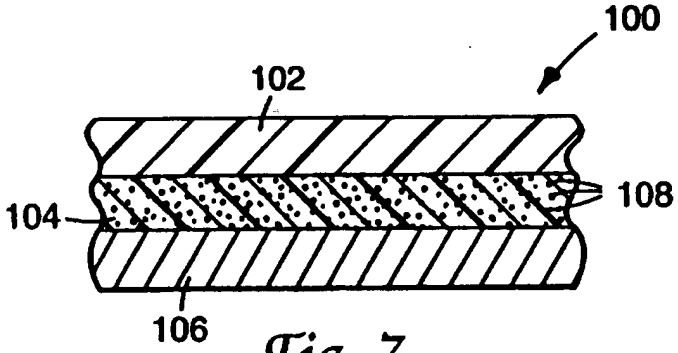

Fig. 7

INTERNATIONAL SEARCH REPORT

Intern al Application No
PCT/US 95/16993

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C08F2/50 A61B5/0408

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C08F A61L A61B C08J

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO,A,94 12585 (MINNESOTA MINING AND MANUFACTURING COMPANY) 9 June 1994 cited in the application see claims 1-16 ---	1-25
Y	EP,A,0 676 457 (GRAPHIC CONTROLS CORPORATION) 11 October 1995 see the whole document ---	1-25
Y	EP,A,0 217 205 (MERCK PATENT GMBH) 8 April 1987 see the whole document ---	1-25
A	EP,A,0 341 560 (MERCK PATENT GMBH) 15 November 1989 see page 6; claims 1-8 --- -/--	1

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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1

Date of the actual completion of the international search	Date of mailing of the international search report
27 August 1996	11. 09. 96

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+ 31-70) 340-3016	Permentier, W

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PCT/US 95/16993

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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A	WO,A,93 09713 (MINNESOTA MINING AND MANUFACTURING COMPANY) 27 May 1993 see claims 1-9	1
A	EP,A,0 246 848 (MINNESOTA MINING AND MANUFACTURING COMPANY) 25 November 1987 cited in the application see claims 1-10	1
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PCT/US 95/16993

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